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Malondialdehyde Outperforms Myeloperoxidase in Identifying Obstructive Coronary Artery Disease: A Cross-Sectional Angiographic Study

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ABSTRACT: **Background**: Oxidative stress plays a central role in coronary atherosclerosis. This study evaluated serum malondialdehyde (MDA) and myeloperoxidase (MPO) in relation to the angiographic severity of coronary artery disease (CAD), and assessed their diagnostic performance.

Methods: In this cross-sectional study, 254 patients aged ≥40 years undergoing coronary angiography were classified into five groups: no CAD (Group I, n = 21), non-obstructive CAD (Group II, n = 22), and single-, double- and triple-vessel/left main obstructive CAD (Groups III–V; n = 89, 70 and 52). Disease severity was quantified using the Gensini score. Serum MDA and MPO were measured by ELISA. Statistical analysis included the Kruskal-Wallis test, Spearman's correlation, ordinal logistic regression and receiver operating characteristic (ROC) curve analysis.

Results: Median MDA increased from 75.2 ng/mL in Group I to 242.6 ng/mL in Group V, and MPO from 6.8 to 15.7 ng/mL (both $p < 0.001$). Both markers correlated positively with the Gensini score (MDA $\rho = 0.599$; MPO $\rho = 0.455$; $p < 0.001$), and MDA correlated inversely with HDL-C. On ordinal logistic regression, MDA ($p = 0.001$) and MPO ($p = 0.016$) were independently associated with CAD severity. MDA showed excellent discrimination for CAD versus non-CAD (AUC 0.944; sensitivity 87.6%, specificity 90.5% at ≥116.96 ng/mL) and for obstructive CAD (AUC 0.915), while MPO showed good discrimination (AUC 0.878 and 0.803, respectively).

Conclusion: Serum MDA and MPO rise in a graded manner with the angiographic severity of CAD and are independently associated with disease burden. MDA showed superior diagnostic accuracy and may serve as a useful biomarker for identifying CAD and obstructive coronary disease.

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INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death and disability worldwide, and its burden is rising rapidly in India, where it tends to occur at a younger age and with more extensive coronary involvement [1]. Coronary angiography remains the reference standard for diagnosing CAD and defining its anatomical severity. However, it is invasive, costly, and not free of risk, and many patients who undergo it are found to have normal or non-obstructive coronaries. There is therefore a continuing need for circulating biomarkers that reflect the underlying disease process and help identify patients with significant coronary atherosclerosis.

Atherosclerosis is now recognised as a chronic inflammatory disease of the arterial wall, in which oxidative stress plays a central role from initiation to plaque progression [2]. An imbalance between reactive oxygen species and antioxidant defences leads to oxidative modification of low-density lipoprotein (LDL) in the subendothelial space. Oxidised LDL promotes endothelial dysfunction, monocyte recruitment, and foam cell formation, and it sustains the inflammatory response that drives lesion growth [3].

Malondialdehyde (MDA) is one of the major end products of polyunsaturated fatty acid peroxidation. Because it is relatively stable, it has been widely used as a marker of lipid peroxidation and systemic oxidative stress [4]. Elevated circulating levels of lipid peroxidation products have been reported in patients with CAD and have been shown to predict cardiovascular events in stable coronary disease [5].

Myeloperoxidase (MPO) is a haem peroxidase stored in the granules of neutrophils and monocytes and released on leucocyte activation. It generates hypochlorous acid and other reactive oxidants that oxidise LDL, impair the protective functions of high-density lipoprotein (HDL), consume nitric oxide, and contribute to plaque instability [6]. Circulating MPO has been associated with the presence of angiographically documented CAD [7] and with adverse outcomes in patients presenting with chest pain and acute coronary syndromes [8,9]. MPO and MDA therefore represent two linked aspects of oxidative injury in atherosclerosis: MPO is an enzymatic source of oxidants, and MDA is a downstream product of lipid damage.

Although these markers have been studied individually, less is known about how they change across the full angiographic spectrum of CAD, from normal coronaries through non-obstructive disease to multivessel obstructive disease. This distinction matters clinically, because non-obstructive CAD is itself associated with a higher risk of myocardial infarction than normal coronaries [10]. Few studies have also examined whether MDA and MPO relate to the quantitative burden of atherosclerosis, as measured by the Gensini score [11], independently of conventional risk factors. Their relative diagnostic value for identifying CAD and obstructive disease also needs comparison, particularly in the Indian population.

We therefore aimed to evaluate serum MDA and MPO levels in patients across five angiographic categories of CAD, to assess their correlation with the Gensini score and other biochemical parameters, to determine whether they are independently associated with CAD severity, and to compare their diagnostic performance for discriminating CAD from non-CAD and obstructive from non-obstructive disease.

METHODOLOGY

Study Design

The cross-sectional study had 256 participants who were recruited from the intensive cardiac care unit at Teerthanker Mahaveer Medical College & Research Centre, Moradabad. Approval for the study was granted by the Institutional Ethical Committee of TMMC&RC (TMU/IEC/2024-25/PG/001) and the research was carried out in accordance with the Declaration of Helsinki. Each participant gave written informed consent; those who refused were excluded.

Sample size

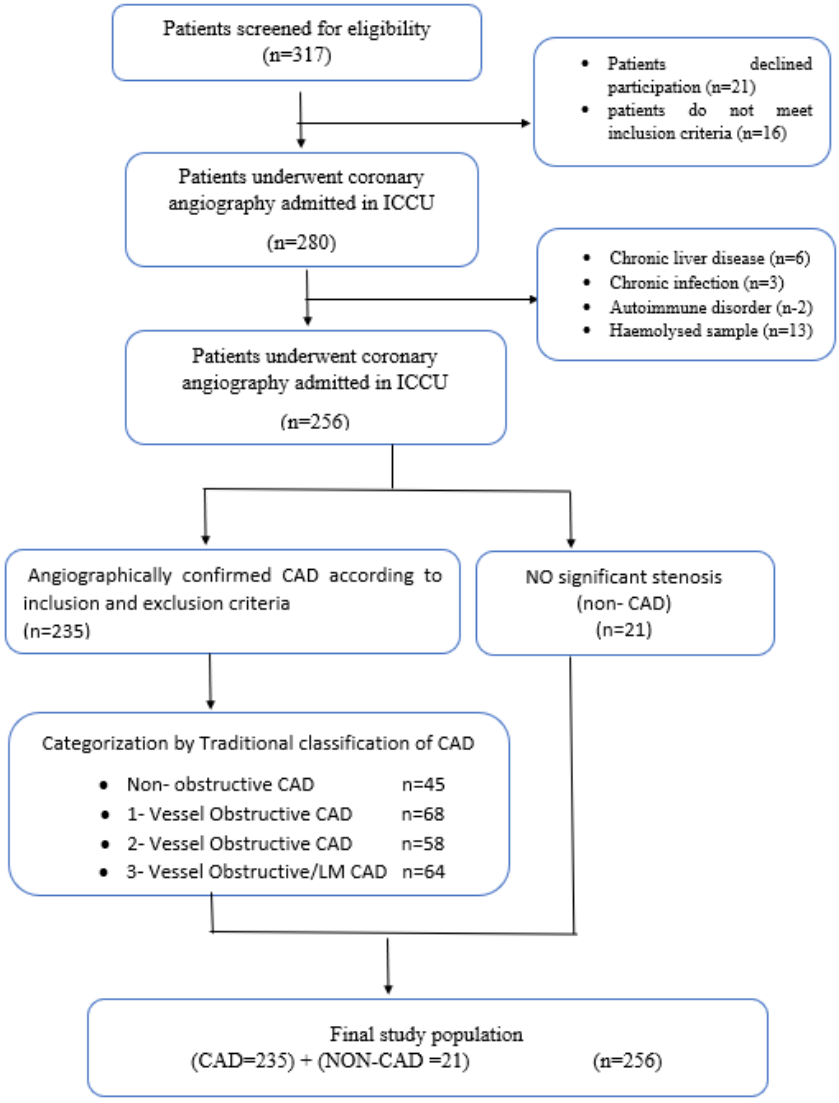
235 angiographically CAD and 21 non- CAD patients were included.

Study population:

Patients who were 40 years of age or older and had CAD which was either confirmed by angiography or suspected on the basis of clinical findings were included. The diagnosed CAD patients and patients with normal coronaries were categorized as group I no CAD (0% stenosis); group II as non-obstructive CAD (1–49% stenosis in any major vessel/branch); group III as 1-vessel

obstructive CAD (≥50% stenosis in 1 major vessel/branch); group IV as 2-vessel obstructive CAD (≥50% stenosis in 2 major vessels/branches); and group V as 3-vessel/LM obstructive CAD (≥50% stenosis in 3 major vessels/branches, or ≥50% stenosis in the left main coronary artery.[12]

The criteria for exclusion include end-stage renal disease or those on dialysis, organ transplant recipients, people with chronic infections (such as TB or HIV/AIDS), individuals with autoimmune or chronic inflammatory conditions (including COPD), those with chronic liver disease or cirrhosis, pregnant women, patients with critical illness or hemodynamic instability, and people who have other major systemic comorbidities apart from metabolic syndrome, diabetes, or familial dyslipidemia. Patients on any medication that alter our results were excluded. [13-15] Written informed consent was taken from all participants before enrolment, and individuals who declined or were unable to provide consent were excluded.



Flowchart 1: Flowchart depicting the selection of the study population.

Blood Collection and Biochemical Evaluation

Following a 12-hour overnight fast, venous blood samples were collected from the antecubital vein into plain vials prior to coronary angiography and any resulting treatment decisions. The collected samples were centrifuged at 3000 rpm for ten minutes to separate the serum, which was then aliquoted and stored at -80°C for a period of approximately 45 days until

laboratory analysis was performed. To avoid repeated freeze-thaw cycles, each aliquot was thawed only once at the time of batch processing.

Standard laboratory methods were used to measure the serum lipid profile comprising total cholesterol, triglycerides, HDL-C, and LDL-C along with CK-MB and NT-proBNP. Serum MDA concentration was determined using a competitive inhibition assay, while MPO levels were quantified through a sandwich ELISA technique. The MDA assay was performed using a commercially available ELISA kit (Catalog No: ELK10897, Lot no: 306317621), with a sensitivity of 9.47 ng/mL and a detection range spanning 31.25–2000 ng/mL. MPO levels were similarly measured using a separate ELISA kit (Catalog No: ELK10187, Lot no: 306316313), offering a sensitivity of 0.65 ng/mL across a detection range of 2.34–150 ng/mL; both kits were sourced from ELK Biotechnology, USA.

Statistical Evaluation:

Data normality was evaluated using the Shapiro-Wilk test. For variables following a normal distribution, comparisons across groups were carried out using ANOVA, whereas the Kruskal-Wallis test was applied to variables that deviated from normality. Depending on the distribution pattern, results were expressed either as mean ± standard deviation or as median with interquartile range. The strength and direction of associations between variables were examined using Spearman's correlation coefficient. To identify factors independently associated with disease severity, multiple linear regression analysis was conducted after adjusting for potential confounders, and diagnostic accuracy was assessed through receiver operating characteristic (ROC) curve analysis. Within the CAD cohort, a multivariable linear regression model was constructed with Gensini Score as the dependent variable, while age, CK-MB, NT-proBNP, triglycerides, LDL-C, HDL-C, MPO, and MDA were entered as independent predictors. Tolerance values and the variance inflation factor (VIF) were used to check for multicollinearity among these predictors. For the ROC analysis, patients were grouped according to the treatment approach received either optimal medical therapy (OMT) or invasive coronary revascularization via percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Statistical significance was defined as a p-value below 0.05, and all analyses were performed using SPSS software, version 26.0.

RESULTS

Table 1: Demographic and clinical profile of study participants stratified by Gensini Score category.

	Group I	Group II	Group III	Group IV	Group V	p-value
No. of patients (n) (%)	21 (8.2%)	22 (8.5%)	89 (34.7%)	71 (27.7%)	53 (20.7%)	--
Age Median (IQR)	53 (45.5-60)	59.5 (51.5–66.0)	55 (49-68)	57.5 (48.0–64.0)	57.0 (50.0–65.0)	0.303
Male (n) (%)	16(76.1%)	18(81.8%)	67 (75.3%)	65 (92.9%)	38 (71.7%)	0.016
Female(n)(%)	5(23.8%)	4(18.2%)	22 (24.7%)	5 (7.1%)	15 (28.3%)	
Smokers (n)	6 (28.5%)	8 (36.4%)	23 (25.8%)	32 (45.7%)	25 (47.2%)	0.034
Hypertension (n)	10(47.6%)	9(40.9%)	42 (47.2%)	24 (34.3%)	22 (41.5%)	0.553
Diabetic (n)	4(19.0 %)	6(27.3 %)	43 (48.3%)	27 (38.6%)	22 (41.5%)	0.090

Gensini score (IQR)	0 --	6.75 (4.0-29.75)	32.0 (24.0–42.5)	50.5 (40.0–68.25)	68.0 (51.0–90.0)	<0.001**
MPO (ng/mL)	6.7 (3.8-9.0)	9.5 (7.9-13.6)	13.6(9.8-16.7)	14.9(10.4-22.8)	16.0(11.7-25.9)	<0.001**
MDA (ng/mL)	75.2(55.2-97.5)	111.0(87.1-119.6)	156.6(132.5-204.7)	205.5(146.5-298.3)	244.8(181.96-332.6)	<0.001**
TC (mg/dL)	166 (141.8 – 177.1)	185.5 (174.4 – 239.0)	196 (179 - 850)	194.9 (165.7-222.2)	233.8 (180.5 257.5)	<0.001**
TG (mg/dL)	128 (112.7 – 153.2)	195 (142.0 – 216)	203 (171.7 – 241.7)	224 (186.7 – 270.7)	238 (205.7 – 294.0)	<0.001**
HDL-C (mg/dL)	46 (39.0- 49.5)	39.5 (38.8-44.0)	36.8 (33.80 – 40.0)	35.0 (31.0 – 37.07)	32.6 (31.0 – 36.0)	<0.001**
LDL-C (mg/dL)	89.4 (75.0 – 111.1)	103.7 (93.9 – 125.8)	118.0 (93.9 – 148.3)	114.9 (93.6–147.3)	150.4 (91.0-178.5)	<0.001**
CK-MB (U/L)	17.5 (14.3 – 19.6)	47.4 (37.1 – 95.3)	68 (42.6 – 95.6)	64.6 (48.9 – 110.9)	60 (37.3 – 94.5)	<0.001**
NT-PRO BNP (pg/mL)	156 (117.5 – 196.5)	387 (264 – 689)	1246 (803 – 1585)	2122 (1170 – 3241)	3245 (1929.2 – 4265)	<0.001**

Demographic characteristics of patients

Table 1 shows the baseline demographic, clinical, angiographic, and biochemical characteristics of the 254 study participants across the five groups: Group I (non-CAD, n = 21), Group II (non-obstructive CAD, n = 22), Group III (single-vessel CAD, n = 89), Group IV (double-vessel CAD, n = 70), and Group V (triple-vessel CAD, n = 52).

Median age was comparable across groups (53.0 to 59.5 years; p = 0.303), so the groups were age-matched. Males predominated in all groups, and the sex distribution differed significantly (p = 0.016), with the highest proportion of males in Group IV (92.9%). The prevalence of smoking also differed significantly (p = 0.034) and was highest in the multivessel groups (45.7% in Group IV and 48.1% in Group V). Hypertension (p = 0.553) and diabetes mellitus (p = 0.090) were not significantly different between groups.

The Gensini score rose progressively with the extent of coronary involvement, from 6.75 in Group II to 68.5 in Group V ($p < 0.001$). Oxidative stress markers followed the same graded pattern. Median MPO increased stepwise from 6.8 ng/mL in Group I to 15.7 ng/mL in Group V, and median MDA from 75.2 to 242.6 ng/mL (both $p < 0.001$), with the highest levels in triple-vessel disease.

Among lipid parameters, TC, TG, and LDL-C were significantly higher, and HDL-C significantly lower, in the CAD groups than in Group I (all $p < 0.001$). HDL-C showed a consistent stepwise decline from Group I (46.0 mg/dL) to Group V (32.8 mg/dL). CK-MB was markedly higher in all CAD groups than in non-CAD participants ($p < 0.001$) but did not rise progressively with the number of vessels involved. NT-proBNP increased steadily with disease severity, from 156 pg/mL in Group I to 3245 pg/mL in Group V ($p < 0.001$).

Overall, increasing angiographic severity of CAD was accompanied by a graded rise in oxidative stress markers (MPO and MDA), atherogenic lipids, and NT-proBNP, and a progressive fall in HDL-C.

Correlation of MDA and MPO with other biochemical parameter

In the pooled population (n = 254), serum MDA showed a strong positive correlation with the Gensini score ($\varrho = 0.599$, $p < 0.001$) and NT-proBNP ($\varrho = 0.534$, $p < 0.001$). It showed moderate positive correlations with TNF-α ($\varrho = 0.406$), HMGB1 ($\varrho = 0.397$), MPO ($\varrho = 0.383$), and CK-MB ($\varrho = 0.317$) (all $p < 0.001$), and a moderate negative correlation with HDL-C ($\varrho = -0.351$, $p < 0.001$). Weak but significant positive correlations were observed with triglycerides, VLDL-C, IL-6, total cholesterol, and LDL-C. MDA did not correlate with age.

Serum MPO in the pooled population correlated moderately and positively with the Gensini score ($\varrho = 0.455$), NT-proBNP ($\varrho = 0.408$), TNF-α ($\varrho = 0.377$), MDA ($\varrho = 0.383$), and HMGB1 ($\varrho = 0.334$) (all $p < 0.001$). It correlated weakly with CK-MB, triglycerides, VLDL-C, and total cholesterol. MPO showed no significant correlation with age, HDL-C, LDL-C, or IL-6.

In the obstructive CAD group (n = 211), both markers remained significantly correlated with angiographic severity (Gensini score: MDA $\varrho = 0.457$, MPO $\varrho = 0.325$; both $p < 0.001$), with inflammatory markers (TNF-α and HMGB1), and with NT-proBNP. MDA also correlated positively with IL-6 and CK-MB and negatively with HDL-C, and MDA and MPO correlated with each other ($\varrho = 0.180$, $p = 0.009$). In non-obstructive CAD, MDA correlated strongly with IL-6 ($\varrho = 0.663$), MPO ($\varrho = 0.500$), and HDL-C (negatively, $\varrho = -0.602$), and moderately with TNF-α ($\varrho = 0.490$). In the non-CAD group, the only significant correlation was between MDA and NT-proBNP ($\varrho = 0.513$, $p = 0.017$).

On subgroup analysis by the number of vessels involved, MDA correlated with the Gensini score in single-vessel ($\varrho = 0.294$) and double-vessel disease ($\varrho = 0.357$). MPO correlated with the Gensini score in double-vessel ($\varrho = 0.320$) and triple-vessel disease ($\varrho = 0.440$).

Table: 2 Ordinal logistic regression (traditional classification)

Dependent variables1221Z	Independent variables	B	S. E	Wald	df	Sig.	95% CI		R squared
							Lower	Upper	
Traditional classification	AGE	-0.018	0.013	1.870	1	0.17	-0.044	0.008	.675
	Gensini Score	0.039	0.008	26.276	1	0.000	0.024	0.054	
	CK-MB	0.001	0.003	0.217	1	0.641	-0.004	0.0006	
	NT-PRO BNP	0.000	0.000	6.842	1	0.009	-0.005	0.000	
	TC	0.003	0.007	0.216	1	0.642	-0.011	0.018	
	TG	0.008	0.003	8.267	1	0.004	0.003	0.014	
	HDL	-0.141	0.029	24.190	1	0.000	-0.198	-0.085	
	LDL	0.009	0.008	1.208	1	0.272	-0.007	0.024	
	HMGB1	0.010	0.011	0.867	1	0.352	-0.012	0.033	
	TNF-alpha	0.018	0.050	0.131	1	0.717	-0.080	0.116	
	IL-6	-0.089	0.049	3.349	1	0.067	-0.185	0.006	
	MPO	0.033	0.014	5.765	1	0.016	0.006	0.060	
	MDA	0.005	0.002	11.961	1	0.001	0.002	0.008	

	HYPERTENSION	0.037	0.272	0.018	1	0.892	-0.496	0.570	
	DIABETES MELLITUS	-0.129	0.279	0.214	1	0.644	-0.676	0.418	
	SMOKING STATUS	-0.099	0.294	0.115	1	0.735	-0.675	0.476	

Ordinal logistic regression analysis (Table 2) showed that, after adjustment for all variables in the model, the Gensini score (B = 0.039, 95% CI 0.024–0.054, p < 0.001), triglycerides (B = 0.008, 95% CI 0.003–0.014, p = 0.004), NT-proBNP (p = 0.009), MPO (B = 0.033, 95% CI 0.006–0.060, p = 0.016), and MDA (B = 0.005, 95% CI 0.002–0.008, p = 0.001) were independently and positively associated with increasing CAD severity by the traditional classification. HDL-C showed a significant inverse association (B = −0.141, 95% CI −0.198 to −0.085, p < 0.001). Age, CK-MB, TC, LDL-C, HMGB1, TNF-α, IL-6, hypertension, diabetes mellitus, and smoking status were not independently associated with CAD severity (all p > 0.05). The model explained 67.5% of the variation in CAD severity (Nagelkerke pseudo R^2 = 0.675), indicating that the oxidative stress markers MPO and MDA are associated with the angiographic severity of CAD independently of conventional risk factors and lipid parameters.

Table 3: Receiver operating characteristic (ROC) curve analysis of serum malondialdehyde (MDA) and myeloperoxidase (MPO) for discriminating coronary artery disease (CAD) and obstructive CAD

Parameters	AUC	95% CI: Lower bound	95% CI: Upper bound	Youden Index (J)	Cut-Off Value	Sensitivity (%)	Specificity (%)	p-Value
CAD vs non-CAD								
MDA	0.944	0.911	0.978	0.781	≥116.96	87.6	90.5	<0.001
MPO	0.878	0.806	0.950	0.608	≥10.12	75.1	85.7	<0.001
Obstructive CAD vs Non-obstructive CAD + non-CAD								
MDA	0.915	0.866	0.964	0.764	≥133.00	83.4	93.0	<0.001
MPO	0.803	0.735	0.871	0.492	≥11.19	67.8	81.4	<0.001
Obstructive CAD vs Non-obstructive CAD								
MDA	0.868	0.783	0.953	0.698	≥133.00	83.4	86.4	<0.001
MPO	0.722	0.623	0.822	0.414	≥10.93	68.7	72.7	<0.001

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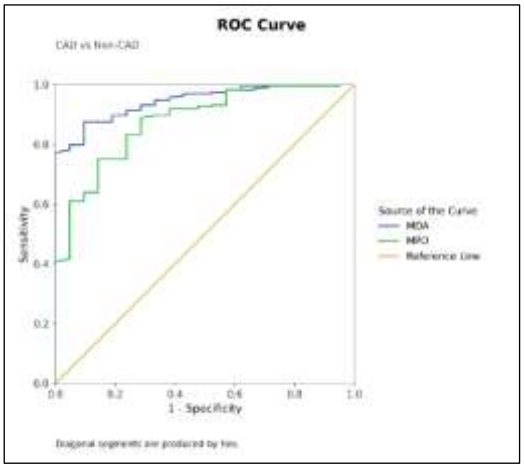


Figure 1 : ROC curves of serum MDA and MPO for discriminating CAD and obstructive CAD

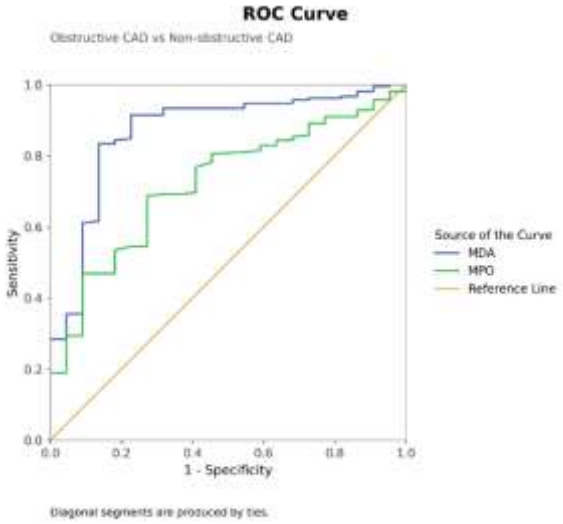


Figure 2 : ROC curves of serum MDA and MPO for discriminating non-obstructive CAD and obstructive CAD

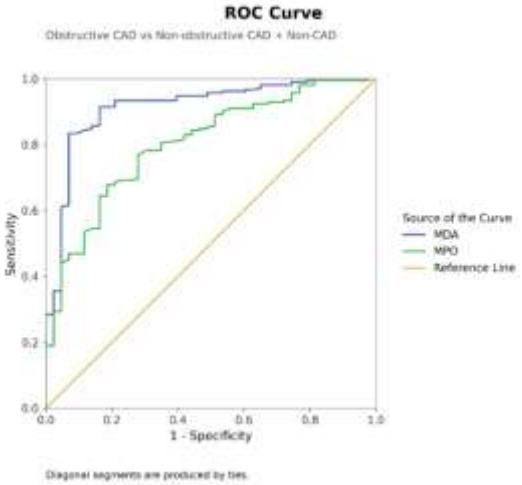


Figure 3: ROC curves of serum MDA and MPO for discriminating obstructive CAD and non-obstructive CAD+ non-CAD

ROC curve analysis (Table 3 and Figure 1,2 and 3) showed that both oxidative stress markers had significant discriminatory ability for CAD, with MDA performing better than MPO in every comparison. For distinguishing CAD from non-CAD, MDA showed excellent diagnostic accuracy (AUC = 0.944, 95% CI 0.911–0.978, $p < 0.001$), with a sensitivity of 87.6% and a specificity of 90.5% at a cut-off of ≥116.96 ng/mL. MPO showed good accuracy (AUC = 0.878, 95% CI 0.806–0.950, $p < 0.001$), with 75.1% sensitivity and 85.7% specificity at a cut-off of ≥10.12 ng/mL. For identifying obstructive CAD against non-obstructive CAD and non-CAD combined, MDA again showed excellent discrimination (AUC = 0.915, 95% CI 0.866–0.964; sensitivity 83.4%, specificity 93.0% at ≥133.00 ng/mL), whereas MPO showed good discrimination (AUC = 0.803, 95% CI 0.735–0.871; sensitivity 67.8%, specificity 81.4% at ≥11.19 ng/mL). When obstructive CAD was compared with non-obstructive CAD alone, MDA retained good diagnostic performance (AUC = 0.868, 95% CI 0.783–0.953; sensitivity 83.4%, specificity 86.4% at ≥133.00 ng/mL), while MPO showed fair discrimination (AUC = 0.722, 95% CI 0.623–0.822; sensitivity 68.7%, specificity 72.7% at ≥10.93 ng/mL) (all $p < 0.001$). These findings suggest that MDA is a stronger marker than MPO for both the presence and the obstructive severity of CAD.

DISCUSSION

In this cross-sectional study of patients who underwent coronary angiography, serum MDA and MPO rose progressively with the angiographic extent of CAD. Both markers correlated with the Gensini score, remained independently associated with CAD severity after adjustment for conventional risk factors and lipid parameters, and discriminated CAD from non-CAD, and obstructive from non-obstructive disease, with good to excellent accuracy. MDA consistently outperformed MPO in these analyses. Taken together, the findings support a close link between oxidative stress and both the presence and the anatomical burden of coronary atherosclerosis.

Oxidative stress is central to atherogenesis. Reactive oxygen species oxidise LDL within the arterial intima, and the oxidised particles are taken up by macrophages to form foam cells, promote endothelial dysfunction, and sustain vascular inflammation. MDA is a stable end product of polyunsaturated fatty acid peroxidation and therefore reflects the cumulative oxidative injury to lipids and cell membranes. In our cohort, median MDA increased more than threefold from the non-CAD group (75.2 ng/mL) to triple-vessel disease (242.6 ng/mL), with a clear stepwise gradient across the intermediate groups. MDA also showed the strongest correlation with the Gensini score of all the parameters examined ($\rho = 0.599$). This graded relationship suggests that lipid peroxidation increases with the anatomical extent of disease rather than being a simple marker of its presence. Our findings agree with earlier work showing that circulating lipid peroxidation products are raised in CAD and predict cardiovascular events in patients with stable disease [5].

MPO is a haem peroxidase released mainly by activated neutrophils and monocytes. It catalyses the formation of hypochlorous acid and other reactive oxidants that modify LDL into an atherogenic form, and it consumes nitric oxide, which impairs endothelium-dependent vasodilation [6]. MPO also oxidises apolipoprotein A-I, the main protein of HDL, which impairs HDL-mediated cholesterol efflux and thereby its anti-atherogenic function [16]. Beyond its role in plaque development, MPO has been implicated in plaque destabilisation through activation of matrix metalloproteinases and promotion of endothelial apoptosis. Elevated MPO has previously been associated with the presence of angiographically documented CAD [7] and with adverse outcomes in patients presenting with chest pain and acute coronary syndromes [8,9]. In our study, MPO rose from 6.8 ng/mL in non-CAD participants to 15.7 ng/mL in triple-vessel disease, and it correlated moderately with the Gensini score ($\rho = 0.455$). The correlation between MPO and the Gensini score was strongest within double- and triple-vessel disease. This may indicate that MPO reflects the greater inflammatory activity and plaque burden of multivessel disease, whereas MDA tracks severity across the whole spectrum.

The significant correlation between MDA and MPO ($\rho = 0.383$ in the pooled population) fits their mechanistic link, since MPO-derived oxidants are an important source of lipid peroxidation in the vessel wall. The two markers also correlated with the inflammatory mediators TNF-α and HMGB1, which supports the concept of an oxidative-inflammatory cycle in atherosclerosis. Inflammatory cytokines activate leucocytes and increase MPO release and reactive oxygen species production. The resulting oxidised lipids and damage-associated molecules such as HMGB1 in turn sustain the inflammatory response. The positive correlation of both markers with NT-proBNP is also notable. It suggests that oxidative stress rises in parallel with myocardial wall stress and ischaemic burden, which grow as coronary involvement becomes more extensive. CK-MB was higher in all CAD groups than in controls but did not increase with the number of diseased vessels. This is consistent with CK-MB reflecting acute myocardial injury rather than the chronic anatomical extent of atherosclerosis.

Among the lipid parameters, HDL-C showed a stepwise decline from the non-CAD group to triple-vessel disease and was inversely correlated with MDA. HDL-C also remained a strong independent protective factor in the regression model. HDL exerts antioxidant effects through associated enzymes such as paraoxonase-1, which hydrolyse lipid peroxides, so low HDL-C may both reflect and contribute to a higher oxidative burden. Triglycerides were independently associated with CAD severity, whereas total cholesterol and LDL-C were not. This may be partly explained by prior statin exposure or by the fact that oxidative modification of LDL, rather than its absolute concentration, determines its atherogenicity.

A key finding is that MDA and MPO remained independently associated with CAD severity after adjustment for age, lipid parameters, cardiac biomarkers, inflammatory markers, hypertension, diabetes, and smoking. Conventional risk factors such as hypertension and diabetes did not differ significantly between groups and were not independent predictors in our model. This suggests that circulating oxidative stress markers may capture aspects of disease activity not reflected by the traditional risk profile.

On ROC analysis, both markers had significant diagnostic value. MDA showed excellent discrimination between CAD and non-CAD (AUC 0.944) and between obstructive CAD and the combined non-obstructive and non-CAD group (AUC 0.915). MPO performed well but less strongly (AUC 0.878 and 0.803). MDA also discriminated obstructive from non-obstructive CAD better than MPO (AUC 0.868 vs 0.722). The better performance of MDA may reflect its nature as a downstream, integrated product of lipid peroxidation from multiple oxidant sources. MPO levels, by contrast, depend on transient leucocyte activation and may fluctuate more within an individual. The ability to distinguish obstructive from non-obstructive disease is clinically relevant, because non-obstructive CAD is itself associated with a higher risk of myocardial infarction than normal coronaries [10]. It also often poses a diagnostic challenge in patients presenting with chest pain. If validated, MDA could complement clinical assessment and non-invasive testing in selecting patients for invasive angiography.

CONCLUSION

In conclusion, serum MDA and MPO increased in a graded manner with the angiographic severity of CAD, correlated with the Gensini score and with inflammatory and myocardial stress markers, and were independently associated with disease severity. MDA showed superior diagnostic accuracy for both the presence and the obstructive severity of CAD, which highlights lipid peroxidation as a promising biomarker of coronary atherosclerotic burden. Larger prospective multicentre studies are needed to validate these findings and establish the prognostic value of these markers.

LIMITATIONS

- First, its cross-sectional design does not allow causal inference or assessment of whether MDA and MPO predict future cardiovascular events.
- It was conducted at a single centre, and the non-CAD and non-obstructive CAD groups were small, which limits the precision of the specificity estimates and of the correlations within these groups.
- The optimal cut-off values were derived and evaluated in the same cohort and therefore require validation in an independent population.
- MDA was measured by ELISA, and absolute values vary considerably across assay methods such as the TBARS assay and HPLC, which limits direct comparison of cut-offs with other studies.
- Antioxidant status and markers of oxidised LDL were not assessed, and residual confounding from medications, smoking intensity, and the higher proportion of men in the multivessel groups cannot be excluded.
- The small size of the non-CAD group (n=21) limited the statistical power and precision of subgroup comparisons and should therefore be interpreted cautiously. Clinical presentation was not stratified in detail, and its potential influence on biomarker levels represents a source of residual confounding.

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